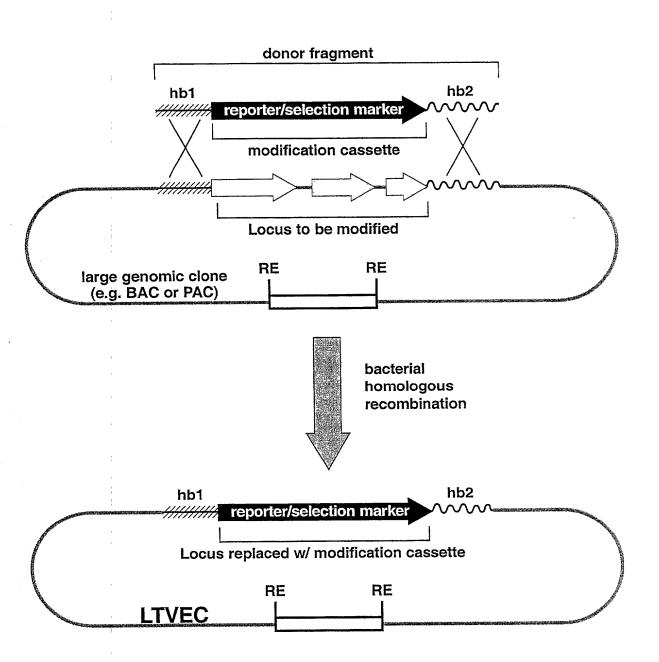
Att. Docket No.: REG 780D

Inventors: Andrew J. Murphy, et al. Title: METHODS OF MODIFYING **EUKARYOTIC CELLS**

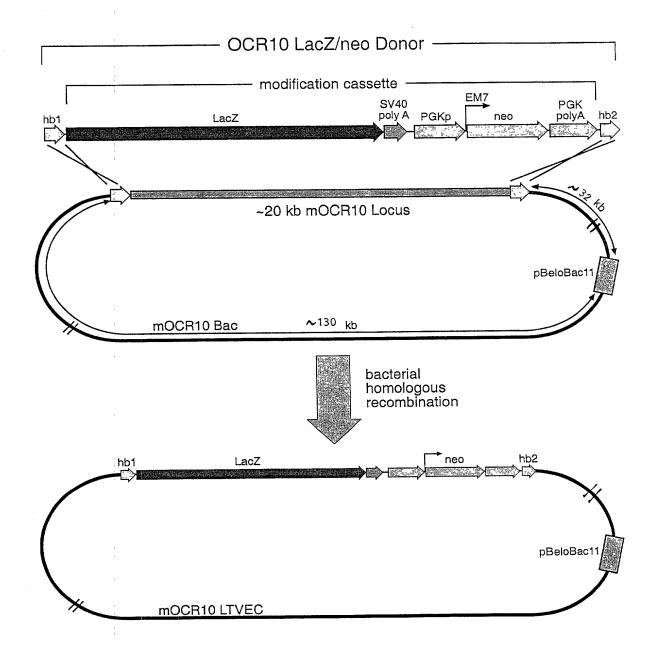
1/7 Figure 1



Att. Docket No.: REG 780D

Inventors: Andrew J. Murphy, et al. Title: METHODS OF MODIFYING EUKARYOTIC CELLS

Figure 2



3/7 FIGURE 3A

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# 4/7

#### FIGURE 3B

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	GCC Arg 860 TGG ACC	CGT Ala AGT TCA	GCG CGC Ala GAC	GGA Pro 870 CCC GGG	GTC Gln GTC CAG	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA	TGA Thr CAG GTC	TCA AGT Ser ACC TGG	TTC AAG Phe BS CAG GTC	TCC Arg. 90 GCT CGA	GGG GJA CCC	ACC TGG Thr	ACC Trp 300 CCC GGG	TCA Ser GAG CTC	CTC Glu> GCA CGT
	GCC Arg 860 TGG ACC	CGT Ala AGT TCA	GCG CGC Ala GAC	GGA Pro 870 CCC GGG	GTC Gln GTC CAG	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA	TGA Thr CAG GTC	TCA AGT Ser ACC TGG	TTC AAG Phe BS CAG GTC	TCC Arg. 90 GCT CGA	GGG GJA CCC	ACC TGG Thr	ACC Trp 300 CCC GGG	TCA Ser GAG CTC	CTC Glu>
	GCC Arg 860 TGG ACC Trp	AGT AGT TCA Ser	GCG CGC Ala GAC	GGA Pro 870 CCC GGG Pro	GTC Gln GTC CAG Val	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln	TCA AGT Ser ACC TGG	TTC AAG Phe BS CAG GTC	TCC Arg. 90 GCT CGA Ala	GGG GJA CCC	ACC TGG Thr	ACC Trp 300 CCC GGG	TCA Ser GAG CTC	CTC Glu> GCA CGT
	GCC Arg 860 TGG ACC Trp 910	CGT Ala AGT TCA Ser	GCG CGC Ala GAC CTG Asp	GGA Pro B70 CCC GGG Pro	GTC Gln GTC CAG Val	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln	TCA AGT Ser ACC TGG Thr	TTC AAG Phe BS CAG GTC GIn	TCC Arg 90 GCT CGA Ala 940	GTA GGG GTA GCC	ACC TGG Thr GAG CTC Glu	ACC Trp 300 CCC GGG Pro	TCA Ser GAG CTC Glu	CTC Glu> GCA CGT Ala>
	GCC Arg 860 TGG ACC Trp 910 GGC	AGT TCA Ser	GCG CGC Ala GAC CTG Asp	GGA Pro B70 CCC GGG Pro 9	GTC GIn GTC CAG Val 20 CAC	CCA GGT Pro ATC TAG .Ile	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln 930 CTG	TCA AGT Ser ACC TGG Thr	TTC AAG Phe BS CAG GTC Gln CTG	TCC Arg. 90 GCT CGA Ala 940 GCT	GGG GLY GGG GLY GTC	ACC TGG Thr GAG CTC Glu	ACC Trp 300 CCC GGG Pro ATC	TCA Ser GAG CTC Glu 60 ATT	CTC Glu> GCA CGT Ala> GTC
	GCC Arg 860 TGG ACC Trp 910 GGC CCG	AGT TCA Ser TGG	GCG CGC Ala GAC CTG Asp	GGA Pro B70 CCC GGG Pro 9 CCT GGA	GTC Gln GTC CAG Val 20 CAC GTG	CCA GGT Pro ATC TAG .Ile ATG	GGC CCG Gly 880 TTT AAA Phe CTG	TGA Thr CAG GTC Gln 30 CTG GAC	TCA AGT Ser ACC TGG Thr CTC GAG	TTC AAG Phe BS CAG GTC GIn CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT CGA	GGG GLY GGG GLY GTC CAG	ACC TGG Thr GAG CTC Glu TTG AAC	ACC Trp 300 CCC GGG Pro Si ATC	TCA Ser GAG CTC Glu 30 ATT TAA	CTC Glu> GCA CGT Ala> GTC CAG
	GCC Arg 860 TGG ACC Trp 910 GGC CCG	AGT TCA Ser TGG	GCG CGC Ala GAC CTG Asp	GGA Pro B70 CCC GGG Pro 9 CCT GGA	GTC Gln GTC CAG Val 20 CAC GTG	CCA GGT Pro ATC TAG .Ile ATG	GGC CCG Gly 880 TTT AAA Phe CTG	TGA Thr CAG GTC Gln 30 CTG GAC	TCA AGT Ser ACC TGG Thr CTC GAG	TTC AAG Phe BS CAG GTC GIn CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT CGA	GGG GLY GGG GLY GTC CAG	ACC TGG Thr GAG CTC Glu TTG AAC	ACC Trp 300 CCC GGG Pro Si ATC	TCA Ser GAG CTC Glu 30 ATT TAA	CTC Glu> GCA CGT Ala> GTC CAG
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	GCC Arg 860 TGG ACC Trp 910 GGC CCG Gly	AGT TCA Ser TGG	GCG CGC Ala GAC CTG Asp	GGA Pro B70 CCC GGG Pro 9 CCT GGA	GTC Gln GTC CAG Val 20 CAC GTG	CCA GGT Pro ATC TAG .Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG	TGA Thr CAG GTC Gln CTG GAC Leu	TCA AGT Ser ACC TGG Thr CTC GAG	TTC AAG Phe BS CAG GTC GIn CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT CGA Ala	GGG GLY GGG GLY GTC CAG	ACC TGG Thr GAG CTC Glu TTG AAC	ACC Trp 300 CCC GGG Pro 95 ATC TAG Ile	TCA Ser GAG CTC Glu 30 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG
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	GCC Arg 860 TGG ACC Trp 910 GGC CCG Gly	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG	GGA Pro 870 CCC GGG Pro 9 CCT GGA Pro	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT	CCA GGT Pro ATC TAG .Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln CTG GAC Leu 9 ATC	TCA AGT Ser ACC TGG Thr CTC GAG Leu	TTC AAG Phe BS CAG GTC GIn CTG GAC Leu CTG	TCC Arg. 90 GCT CGA Ala 940 GCT CGA Ala CCT	GCC GLY GGG CCC GLY GTC CAG Val	ACC TGG Thr GAG CTC Glu TTG AAC Leu	ACC Trp 00 CCC GGG Pro 95 ATC TAG Ile	TCA Ser GAG CTC Glu 30 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val>
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	GCC Arg 860 TGG ACC Trp 910 GGC CCG Gly CTG	AGT TGG ACC Trp 960 GTT CAM	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro B70 CCC GGG Pro 9 CCT GGA Pro ATG	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA	CCA GGT Pro ATC TAG .Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG	TGA Thr CAG GTC G1n CTG GAC Leu 9 ATC TAG	ACC TGG Thr CTC GAG Leu 80 CAC GTG	TTC AAG Phe BS CAG GTC GIn CTG GAC Leu CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT CGA Ala CCT GGA	GCC Gly GGG OCC Gly GTC CAG Val P90 TGG ACC	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC	ACC Trp 00 CCC GGG Pro ATC TAG Ile CTA GAT	GAG CTC Glu 30 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val> AAA TTT
	GCC Arg 860 TGG ACC Trp 910 GGC CCG Gly CTG	AGT TCA Ser TGG ACC Trp 960 GTT CAM	GCG CGC Ala GAC CTG Asp CTG Asp	GGA Pro B70 CCC GGG Pro 9 CCT GGA Pro ATG	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly	CCA GGT Pro ATC TAG Lle ATG TAC CTG GAC Leu	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln CTG GAC Leu 9 ATC TAG Ile	ACC TGG Thr CTC GAG Leu BO CAC GTG His	TTC AAG Phe 8: CAG GTC Gln CTG GAC Leu CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT CGA Ala CCT GGA	GGG GGG GCC GLY GTC CAG Val P90 TGG ACC Trp	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00 CCC GGG Pro ATC TAG Ile CTA GAT	GAG CTC Glu ATT TAA Ile 1000 TGG ACC Trp	CTC Glu> GCA CGT Ala> GTC CAG Val> AAA TTT Lys>
	GCC Arg 860 TGG ACC Trp 910 GGC GCG GLY CTG GAC Leu	AGT TCA Ser TGG ACC Trp 960 GTT CAA	GCG CGC Ala GAC CTG Asp CTG Asp	GGA Pro B70 CCC GGG Pro CTA Pro ATG TAC	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly	CCA GGT Pro ATC TAG Lie ATG TAC Met CTG GAC Leu	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln CTG GAC Leu 9 ATC TAG Ile	ACC TGG Thr CTC GAG Leu BO CAC GTG His	TTC AAG Phe 8: CAG GTC GIn CTG GAC Leu CTG GAC Leu	TCC Argonal Ar	GCC Gly GGG CCC Gly GTC CAG Val P90 TGG ACC Trp	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00 CCGG Pro ATC TAG Ile CTAT Leu	TCA Ser GAG CTC Glu 30 ATT TAA Ile 1000 TGG ACC Trp	GTC GTC CAG Val> AAA TTT LYS>
	GCC Arg 860 TGG ACC Trp 910 GGC GCG GLY CTG GAC Leu	AGT TCA Ser TGG ACC Trp GGT CAA Val	GCG CGC Ala GAC CTG Asp CTG Asp	GGA Pro B70 CCGG Pro CTA Pro ATGC Met	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly 1	CCA GGT Pro ATC TAG Lie ATG TAC CTG GAC Leu 020 GTG	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln CTG GAC Leu 9 ATC TAG Ile ACC	ACC TGG Thr CTC GAG Leu 80 CAC GTG His	TTC AAG Phe 8: CAG GTC Gln CTG GAC Leu CTG GAC	TCC Arg. 90 GCT CGA Ala 940 GCT Ala CCT AGA Pro	GCC Gly GGG CCC Gly GTC CAG Val P90 TGG ACC TTP 100	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00 CGG o Pr 0: ATAG Ile CTAT Leu CAG	GAG CTC Glu ATT TAA Ile 1000 ACC TTP CCC	GTC GTC CAG Val> AAA TTT LYS> 050 CTG
	GCC Arg 860 TGG ACC Trp 910 GGC GCG GLY CTG GAC Leu AAG	AGTA TCA Ser TGG ACC Trp GGTT CAA Val ATA	GCG CGC Ala GAC CTG Asp CTTC AAG Phe	GGA Pro B70 CCC GGG Pro GCA Pro ATG TAC Met	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly 1	CCA GGT Pro ATC TAG Lie ATG TAC Met CTG GAC Leu 020 GTG CAC	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC GIn CTG GAC Leu ATC TAG TAG TGG	ACC TGG Thr CTC GAG Leu 80 CAC GTG His 1030 CCT GGA	TTC AAG Phe B: CAG GTC GIn CTG GAC Leu CTG GAC Leu GAG CTC	TCC Arg. PO GCT CGA Ala 940 GCT CGA Ala CCT GGA Pro AGT TCA	GGG GGC GLY GTC GAG Val PGGG ACC Trp 100 AAG	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00CGG0 PrOCGTATILE CTATILE CACC CACC CACC CACC CACC CACC CACC CA	GAG CTC Glu 30 ATT TAA Ile 1000 TGG ACC Trp CCG	GTC GAG Val> AAA TTT LYS> 050 CTG GAC
	GCC Arg 860 TGG ACC Trp 910 GGC GCG GLY CTG GAC Leu AAG	AGTA TCA Ser TGG ACC Trp GGTT CAA Val ATA	GCG CGC Ala GAC CTG Asp CTTC AAG Phe	GGA Pro B70 CCC GGG Pro GCA Pro ATG TAC Met	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly 1	CCA GGT Pro ATC TAG Lie ATG TAC Met CTG GAC Leu 020 GTG CAC	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC GIn CTG GAC Leu ATC TAG TAG TGG	ACC TGG Thr CTC GAG Leu 80 CAC GTG His 1030 CCT GGA	TTC AAG Phe B: CAG GTC GIn CTG GAC Leu CTG GAC Leu GAG CTC	TCC Arg. PO GCT CGA Ala 940 GCT CGA Ala CCT GGA Pro AGT TCA	GGG GGC GLY GTC GAG Val PGGG ACC Trp 100 AAG	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00CGG0 PrOCGTATILE CTATILE CACC CACC CACC CACC CACC CACC CACC CA	GAG CTC Glu 30 ATT TAA Ile 1000 TGG ACC Trp CCG	GTC GTC CAG Val> AAA TTT LYS> 050 CTG

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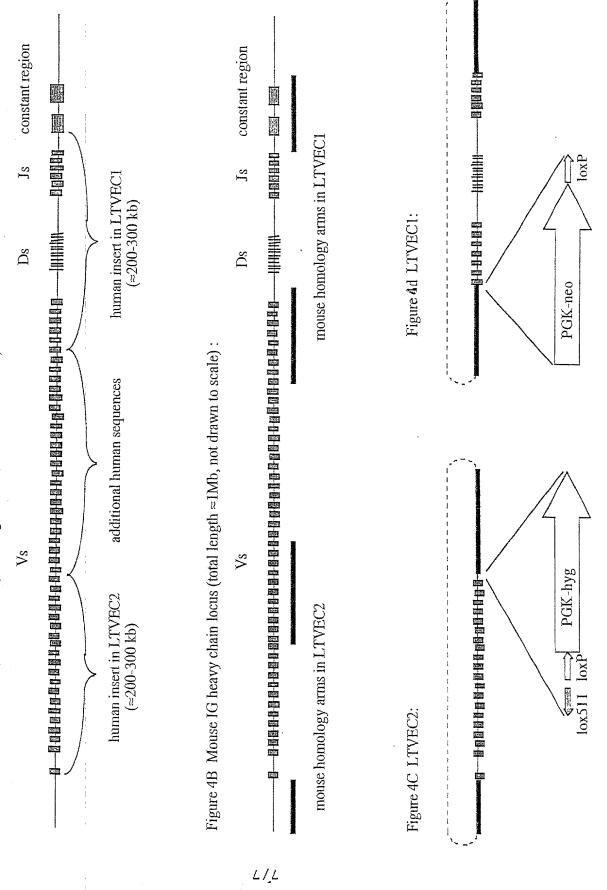
FIGURE 3C

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	-		GGT			GAG	CAA			TGT			A TO CE			CCT	
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		12	50		1:	260			1270			12	3 D		1:	290	
														GTC			
														CAG			
	Gly	His	Trp	Cys	Ile	Ile	Pro	Leu	Ala	Ala	Gly	Gln	Ala	Val	Ser	Ala>	
	m 2 C	i	1300		T C T	13.		~~~		320	ama		1330		~-~	* G *	
											1.111-	(5) I (5)				Δ('Δ	
'			GAG														
,	ATG	TCA	CTC	CTC	TCT	CTG	GCC	GGT	ATA	CCA	GAC	CAC	AGG	TAA	CTG	TGT	
,	ATG	TCA	CTC	CTC	TCT	CTG	GCC	GGT	ATA	CCA	GAC	CAC	AGG	TAA	CTG		
1.3	ATG Tyr	TCA	CTC	CTC	TCT	CTG Asp	GCC	GGT Pro	ATA	CCA	GAC	CAC	AGG Ser	TAA	CTG	TGT	
1.3	ATG Tyr 340	TCA	. CTC Glu 1	: CTC : Glu :350	TCT Arg	CTG Asp	GCC Arg 1360	GGT Pro	ATA Tyr	CCA Gly 13	GAC Leu 70	CAC Val	AGG Ser 1	TAA Ile 380	CTG Asp	TGT	
13	ATG Tyr 340 GTG	TCA Ser ACT	CTC Glu 1 GTC	CTC Glu .350 GGA	TCT Arg	CTG Asp GCA	GCC Arg 1360 GAG	GGT Pro	ATA Tyr CTG	CCA Gly 13 TGT	GAC Leu 70 GTC	CAC Val TGG	AGG Ser 1 CCC	TAA Ile 380 TGT	CTG Asp AGC	TGT Thr>	
13	ATG Tyr 340 GTG CAC	TCA Ser ACI	CTC Glu 1 GTG CAC	CTC Glu .350 GGA CCT	TCT Arg GAT	CTG Asp GCA CGT	GCC Arg 1360 GAG CTC	GGT Pro GGC CCG	ATA Tyr CTG GAC	CCA Gly 13 TGT ACA	GAC Leu 70 GTC CAG	CAC Val TGG ACC	AGG Ser 1 CCC GGG	TAA Ile 380 TGT ACA	CTG Asp AGC TCG	TGT Thr>	
13	ATG Tyr 340 GTG CAC Val	F ACT	CTC Glu 1 GTG CAC	CTC Glu .350 GGA CCT LGly	TCT Arg GAT CTA Asp	CTG Asp GCA CGT	GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly	ATA Tyr CTG GAC	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val	CAC Val TGG ACC Trp	AGG Ser 1 CCC GGG	TAA Ile 380 TGT ACA Cys	CTG Asp AGC TCG Ser	TGT Thr> TGT ACA	
13	ATG Tyr 40 GTG CAC Val	F TCA Ser ACT TGA Thi	CTC Glu Glu CGC CGC CGC CGC CGC CGC CGC CGC CGC C	CTC Glu .350 GGA CCT LGly	TCT Arg GAT CTA Asp	CTG Asp GCA CGT Ala	GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly 410	ATA Tyr CTG GAC Leu	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val	CAC Val TGG ACC TTP	AGG Ser 1 CCC GGG Pro	TAA Ile 380 TGT ACA Cys	CTG Asp AGC TCG Ser	TGT Thr> TGT ACA Cys>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC	G ACT G ACT Thi	CTC Glu 1 GTG CAC Val	CTC Glu .350 GGA CCT LGly 14	TCT Arg GAT CTA Asp	CTG Asp GCA CGT Ala	GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly 410 ATG	ATA Tyr CTG GAC Leu	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val 1420 GAT	TGG ACC Trp	AGG Ser 1 CCC GGG Pro	TAA Ile 380 TGT ACA Cys 14 AGA	CTG Asp AGC TCG Ser 30 GAG	TGT TGT ACA Cys> TCT	
13	ATG TYT 40 GTG CAC Val 1390 GAC CTG	F ACT	CTC Glu GTG CAC Val GATA A CTA	CTC Glu .350 GGA CCT LGly 14 GGC ACCG	TCT Arg GAT CTA Asp 100 TAT ATA	CTG Asp GCA CGT Ala CCA	GCC Arg 1360 GAG CTC Glu 1 GCC	GGT Pro GGC CCG Gly 410 ATG	ATA Tyr CTG GAC Leu AAC	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val 1420 GAT CTA	TGG ACC Trp GCT CGA	AGG Ser 1 CCC GGG Pro	TAA Ile 380 TGT ACA Cys 14 AGA TCT	CTG Asp AGC TCG Ser 30 GAG CTC	TGT ACA CYS>	
13	ATG TYT 40 GTG CAC Val 1390 GAC CTG	F ACT	CTC Glu GTG CAC Val GAT A CTA	CTC Glu .350 GGA CCT LGly 14 GGC ACCG	TCT Arg GAT CTA Asp 100 TAT ATA	CTG Asp GCA CGT Ala CCA	GCC Arg 1360 GAG CTC Glu 1 GCC	GGT Pro GGC CCG Gly 410 ATG	ATA Tyr CTG GAC Leu AAC	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val 1420 GAT CTA	TGG ACC Trp GCT CGA	AGG Ser 1 CCC GGG Pro	TAA Ile 380 TGT ACA Cys 14 AGA TCT	CTG Asp AGC TCG Ser 30 GAG CTC	TGT TGT ACA Cys> TCT	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG	F ACT	CTC Glu GTG CAC Val GAT A CTA	CTC Glu .350 GGA CCT LGly 14 GGC ACCG	TCT Arg GAT CTA Asp 100 TAT ATA	CTG Asp GCA CGT Ala CCA GGT	GCC Arg 1360 GAG CTC Glu 1 GCC	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA Tyr CTG GAC Leu AAC	CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp	TGG ACC Trp GCT CGA	AGG Ser 1 CCC GGG Pro GGC CCG	TAA Ile 380 TGT ACA Cys 14 AGA TCT AYG	CTG Asp AGC TCG Ser 30 GAG CTC	TGT ACA CYS> TCT AGA Ser>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG	G ACT C TGA C TGA C TGA C TAI C TAI C ASI	CTC Glu GTG CAC Val GAT GAT A CTM A Spring	GOTC Glu .350 GGA COT L Gly 14 F GGC A CCG	TCT Arg GAT CTA Asp 100 TATA ATA TYI	CTG Asp GCA CGT Ala CCA GGT	GCC Arg 1360 GAG CTC Glu 1 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA TYT CTG GAC Leu AAC TTG Asn	CCA Gly 13 TGT ACA Cys CTG GAC	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp	TGG ACC Trp GCT CGA Ala	AGG Ser 1 CCC GGG Pro GGC CCG Gly	TAA Ile 380 TGT ACA Cys 144 ACA ACA	AGC TCG Ser 30 GAG CTC Glu	TGT ACA CYS> TCT AGA Ser>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG	G ACT C TGA C TAIL C TA	CTC Glu GTG CAC Val GAT A CTM A CTM A ASI	CTC Glu .350 GGA CCT LGly 14 LGCG CGC CGC CGC	TCT Arg GAT Asp 100 TATA ATA TYX	CTG ASP GCA CGT Ala CCA GGT Pro	GCC Arg 1360 GAG CTC Glu 1 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA TYT CTG GAC Leu AAC TTG Asn	CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp	TGG ACC Trp GCT CGA Ala	AGG Ser 1 CCC GGG Pro GGC CCG Gly	TAA Ile 380 TGT ACA Cys 14 AGA TCT ATG	AGC TCG Ser 30 GAG CTC Glu	TGT Thr> TGT ACA Cys> TCT AGA Ser>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG GC GC	G ACT C TGA C TGA C TGA C TA C T	CTC Glu GTG CAC Val GAT A CTM A ASP	CTC	GATT CTA GATA ASP TATA ATA ATA AGAG	CTG ASP GCA CGT Ala CCA GGT Fro	GCC Arg 1360 GAG CTC Glu 1 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA TYT CTG GAC Leu AAC TTG AST	CCA Gly 13 TGT ACA Cys CTG GAC Leu GAC CAG	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP	TGG ACC Trp GCT CGA Ala	AGG Ser 1 CCC GGG Pro GGC GLY CCT GGA	TAA Ile 380 TGT ACA Cys 14 AGA TCT AXG	AGC TCG Ser 30 GAG CTC Glu	TGT ACA CYS> TCT AGA Ser>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG GC GC	G ACT G ACT Thi C GAT C CTX A Asi 1440 T CCX A GG;	CTC Glu GTG CAC CAC CAC CAC CAC CAC CAC CAC CAC CA	CTC	TCT Arg GAT CTA ASP ATA TYI	CTG ASP GCA CGT Ala CCA GGT Pro	GCC Arg 1360 GAG CTC Glu 1 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA TYT CTG GAC Leu AAC TTG ASN 60 TTG AAC	CCA Gly 13 TGT ACA Cys CTG GAC Leu CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP	TGG ACC Trp GCT CGA Ala 470 GAC CTG Asp	AGG Ser 1 CCGGG Pro GGC GCG G1y CCT GGA	TAA Ile 380 TGT ACA Cys 14 AGA TCT AXG	AGC TCG Ser 30 GAG CTC Glu 1480 TTT AAAA Phe	TGT ACA Cys> TCT AGA Ser> CTG GAC Leu>	
13	ATG TYT 40 GTG CAC Val 1390 GAC GTG GCC GCC GCC GCC	G ACT G ACT Thi C GAT C CTX A SG A GG Y Pr	CTC Glu GTG CAC CAC CAC CAC CAC CAC CAC CAC CAC CA	CTC Glu .350 GGA CCT LGIY LGIY CGC ACCG ACCG ACCG ACCG ACCG ACCG ACCG	TCT Arg	CTG Asp GCA CGT Ala CCA GGT Pro CTA CTA CTA	GCC Arg 1360 GAG CTC Glu 1 CCGG Ala CCTG CAC	GGT Pro GGC CCG Gly 410 ATG TAC Met	ATA TYT CTG GAC Leu AAC TTG Asn 60 TTG AAC Leu 1510	CCA Gly 13 TGT ACA Cys CTG GAC Leu GAC Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP 1 ACA TGT Thr	TGG ACC Trp GCT CGA Ala 470 GACC CTG	AGG Ser 1 CCGGG Pro CGG Gly CCT GGA Pro	TAA Ile 380 TGT ACA Cys 14 AGA TCT ACG ACGA	AGC TCG Ser 30 GAG CTC Glu 1480 TTT AAAA Phe	TGT ACA CYS> TCT AGA Ser> CTG GAC Leu>	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG GCC GCC GCC TC	G TCA Ser Ser TGA Thr C GAN L Asi L Asi L Asi L Asi L Asi T CG T TG	CTC Glu GTG CAC CAC CAC CAC CAC CAC CAC CAC CAC CA	C TC	TCT Arg GAT CTA ASP ATA GAG GAT GAT GAT GAT GAT GAT GAT GAT	CTG Asp GCA CGT Ala CCA GGT Pro CTA CTA CTA CTA CTA CTC	GCC Arg 1360 GAG CTC Glu 1 GCC CGG Ala CTG CAG CAG CAG CAG CAG CAG CAG CAG CAG CA	GGT Pro GGC CCG Gly 410 ATG TAC Met CTC GAG	ATA TYT CTG GAC Leu AAC ASS ASS Leu 1510 GGC	CCA Gly 13 TGT ACA Cys CTG GAC Leu CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp 1 ACA TGT Thr	TGG ACC Trp GCT CGA Ala 470 CTG ASp 15	AGG Ser 1 CCC GGG Pro GGC G1y CCT GGA Pro	TAA Ile 380 TGT ACA Cys 14 AGA TCT ACG ACG GGC	AGC TCG Ser 30 GAG CTC Glu 1480 Phe	TGT ACA CYS> TGT AGA Ser> CTG GAC Leu> 530	
13	ATG Tyr 340 GTG CAC Val 1390 GAC GTG GCC GCC GCC AG	G TCA Ser Ser TGA Thr C GAN L Asi L 440 C GC L Asi T GC T GC T TGA	CTC Glv GTG CAC CAC T CAC T CAC T CAC T A CTM A CTM A CTM A CTM A CTM A CTM C Asi C CC T CGC A CC T CGC A CC	CTC. CTC. CTC. CTC. CTC. CTC. CTC. CTC.	TCT Arg	CTG Asp GCA CGT Ala CCA GGT Pro GGAT CTA L500 CTCA GGAT L500	GCC Arg 1360 GAG CTC Glu 1 CCGG Ala CCTG CAG CCGG Ala CCTG CCG CCG CCGG CCG CCG CCG CCG CCG C	GGT Pro GGC CCG Gly 410 ATG TAC Met CTC	ATA TYT CTG GAC Leu AAC TTG Asn 60 TTG Leu 151(TGGT A CC/ A CC/	CCA Gly 13 TGT ACA Cys CTG GAC Leu CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp 11 ACA TGT Thr	TGG ACC Trp GCT CGA Ala 470 CTG ASp 15 CTT GAA	AGG Ser 1 CCGG Pro GGC G1y CCT GGA Pro 20	TAA Ile 380 TGT ACA Cys 14 AGA TCT ATG CGA ATG ATG	AGC TCG Ser 30 GAG CTC Glu 1480 Phe 1 TCG AGG	TGT ACA CYS> TCT AGA Ser> CTG GAC Leu>	

6/7 Figure 3D

1540					155	0		1560			•	1570				
GGC													GAA	GGG	GAC	
CCG	TCG	GAT	GAC	CTG	TCC	AAC	TCC	GAC	AGT	AAA	CGT	TTC	CTT	caa	CTG	
Gly	Ser	Leu	Leu	Asp	Arg	Leu	Arg	Leu	Ser	Phe	Ala	Lvs	Glu	Glv	Asp>	
	:															
	1590															
													GGG			
													ccc			
Trp	Thr	Ala	Asp	Pro	Thr	Trp	Arg	Thr	Gly	Ser	Pro	Gly	Gly	Gly	Ser>	
	30 1640 AG AGT GAA GCA GGT															
													TGT			
Glu	Ser	Glu	Ala	Gly	Ser	Pro	Pro	Gly	Leu	Asp	.Met	Asp	Thr	Phe	Asp>	
													:			
															GAA	
													TGA			
Ser	GTĀ	Pne	Ala	GTĀ	ser	Asp	Cys	GTA	Ser	Pro	Val	Glu	Thr	Asp	Glu>'	
	1730 1							1750			3960			1770		
CCA															CCA	
													TGG			
															GGT Pro>	
ييت	1 4 0	***	Y	044		2000	B	13 mag	ني نه نه	VEL	Val	m g	1177	FIO	P10>	
		1780			17	90		1800								
CCT					GCC											
	1				CGG											
					Ala					>						

Figure 4A Human Ig heavy chain locus (total length ≈1Mb, not drawn to scale):



EUKARYOTIC CELLS Inventors: Andrew J. Murphy, et al. Title: METHODS OF MODIFYING Title: METHODS OF MODIFYING Title: METHODS OF MODIFYING